Social Adaptive Functioning, Apathy, and Nondysphoric Depression among Nursing Home-Dwelling Very Old Adults

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Key Words

Nondysphoric depression · Late-life psychiatry · Cognitive impairment · Nursing home · Psychosocial adaptation · Apathy

Abstract

Background: Apathetic and subsyndromal depressive conditions are common in the oldest old. This study examined whether nondysphoric depression (NDD), a clinical condition characterized by ideational and vegetative but no emotional symptoms of depression, belongs to the apathetic presentations of late-life depression. Rates of NDD, dysphoric depression (DD), apathy, and social functional impairment were examined in a sample of nondemented very old (mean age 87.5 years, SD = 7.7) nursing home residents. It was hypothesized that individuals with NDD show greater apathy and greater social functional impairment relative to DD and nondepressed individuals. **Methods:** Social functioning was measured using the Social-Adaptive Functioning Evaluation (SAFE) and apathy was measured using the global apathy rating on the Scale for the Assessment of Negative Symptoms (SANS). **Results:** The rates of DD (50.0%) and NDD (27.4%) were quite high. Participants with DD reported greater apathy than those with NDD (and nondepressed individuals). NDD and DD subjects showed greater social functional impairment relative to the comparison group. There was no difference in social functioning between DD and

NDD individuals. **Conclusions:** The present data are inconsistent with the view that NDD among the oldest old is an apathetic form of depression. NDD involves social functional impairment. Limitations include rather selected population of nursing home residents that may have included individuals with early dementia, lack of data on prior depressive episodes, and apathy assessment not validated on the specific population.

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In the field of medicine, atypical, incomplete, or attenuated manifestations of diseases are often termed *forme fruste* (from the French ‘unfinished’). Similarly, some individuals seeking clinical attention report depressive symptoms in insufficient number to meet the diagnostic criteria for major depression [1, 2] [3, p. 183]. The DSM-5 also contemplates depressive symptoms causing clinically significant distress or impairment in social or occupational functioning, not meeting the criteria for major depression or any other mood disorder class (e.g. unspecified depressive disorder) [3]. Recently attention has been drawn to the fact that syndromic clusters of ideational (e.g. guilt) and vegetative (e.g. poor sleep or fatigue) depressive symptoms but at best inconsistent reporting of affective symptoms (nondysphoric depression; NDD) may have psychiatric significance and be present in excess among older adults [4–8]. The exact nature of

this clinical condition is currently not fully known. The present report represents an initial effort to clarify its boundaries with another common psychopathological aspect of late life: apathy.

Among older adults, medical conditions often present as *forme fruste*. For example, myocardial infarction may present without excruciating pain [9], or pneumonia may show little fever [10]. NDD may be one of the incomplete depressive syndromes [4, 11, 12] common in later life [5, 13–15]. Alternatively, NDD may be a form of depression influenced by the simultaneous presence of other psychopathology (i.e. apathy). In late life, apathy (or reduced motivation or lack of initiative and exploration) may occur commonly as a sole psychopathological feature [16, 17]. It is also widely acknowledged that apathy may be a common symptom of depression [17–22]. Older depressed individuals with significant apathy may participate poorly in clinical exams, thereby showing a reduced endorsement of sadness [18]. The phenomenological presentation of depression (ascertained during the mental state examination aspect of the clinical exam) may henceforth be altered if patients with significant apathy only erratically report sadness and diminished hedonic capacities (i.e. dysphoria) but nonetheless consistently report clusters of vegetative and ideational depressive symptoms [2]. Hence, the question arises of whether in later life NDD is an attenuated (*forme fruste*) depression or a depression the presentation of which is significantly influenced by the presence of apathy.

Depression is associated with diminished psychosocial adjustment or social functional adaptation [23–25]. Social functional adaptation has been described as covering the patient's role performance, social competence, self-care, impulse control, and cooperativeness or interpersonal relationships as well as life skill functioning [26]. Poor social engagement has been reported in late-life depression [25]. Though the association between social functional adaptation and depression has been reported in nursing home dwellers [27], the relationship between NDD and social functional adaptation in nursing home patients is not known.

The present study examined the rates of dysphoric depression (DD) and NDD among older adults living in nursing homes. Along with elevated rates of DD [15, 20, 28–30], it was expected that rates of NDD would be higher among this group than community-dwelling and younger populations [4, 6, 11, 31]. The first aim of the present study was to describe the association of NDD with apathy. A second aim of this study was to determine whether NDD and DD among the oldest old have differing effects on social functional adaptation.

Methods

Study Sample

The sample of subjects examined in this study has been described in previous reports [32–34] and consisted of residents of rural nursing homes in the state of Iowa, USA. The nursing homes considered for the present study are staffed by the University of Iowa Geriatric Psychiatry Division. Three nursing homes were selected out of about 400 in the state of Iowa based on convenience and proximity to the University. The study participants were assessed by an experienced research assistant trained at the Iowa Mental Health Clinic Research Center directed by N.C. Andreasen. All participants were comprehensively assessed for psychiatric/behavioral symptoms and cognitive and functional status. The inclusion criteria in the parent study [33, 34] were age over 65 years and being a long-term resident of a nursing home. The exclusion criteria were a history of schizophrenia, bipolar disorder, and mental retardation, and severe cognitive impairment, unavailability of the decision maker, and inability to cooperate (e.g. aphasia). Informed consent was obtained from the subjects or their legal representatives after the study protocol, as approved by the University of Iowa Human Subjects Committee, had been discussed. Twenty-three subjects (out of 69) had their legal representatives sign the consent form after giving verbal consent, while the rest (46 subjects) completed and signed the consent form themselves. Sixty-two subjects (or 89.9%) were able to cooperate with a depression assessment and constituted the study sample.

Measurement Instruments

The medical and psychiatric history including medications was obtained by reviewing the medical records (e.g. clinical progress notes and laboratory measures) and confirmed by interviewing the participants and nursing staff. Depression was assessed using the Hamilton Depression Rating Scale (Ham-D) [35]. Cognitive functioning was measured using Folstein's Mini-Mental State Exam (MMSE) [36]. Apathy was measured using the global apathy rating on the Scale for the Assessment of Negative Symptoms (SANS) [37]. The SANS has good reliability and validity [37]. Apathy is rated using a 5-point scale [0 = no evidence of (1) poor grooming or hygiene, (2) impersistence (or inability to sustain an action), and (3) physical energy, avolition, or apathy; 1 = questionable; 2 = mild; 3 = moderate, and 4 = severe; analyses were carried out using the global score]. Ability in social and daily living skills was measured using the Social-Adaptive Functioning Evaluation (SAFE), a scale with good reliability and validity for assessing living skills in later life [38]. SAFE is a 17-item rating scale that assesses social competence and adjustment, self-care, impulse control, and cooperativeness and life skill functioning. Each item is rated on a 5-point scale (0 = no impairment, 1 = mild impairment, 2 = moderate impairment, 3 = severe impairment, and 4 = extreme impairment). Higher scores reflect more severe impairment. The possible total score range is 0–68.

Variables

Subjects were categorized as DD, NDD, or nondepressed (ND) comparison participants following the criteria of prior research [4, 8], and symptoms were assessed using the Ham-D [35]. Subjects were categorized as NDD if they admitted to one the following ideational symptoms of depression: guilt, self-depreciation, worthlessness, pessimism, or sense of failure, and 2 or more vegetative

Table 1. Demographic and clinical characteristics

Variable	NDD	DD	ND
Mean age $\pm$ SD, years	88.4 $\pm$ 6.8	83.7 $\pm$ 8.6	88.6 $\pm$ 6.0
Females	15 (83.2)	24 (78.4)	11 (78.6)
Mean education $\pm$ SD, years	13.8 $\pm$ 2.1	12.0 $\pm$ 3.1	13.7 $\pm$ 3.1
Mean MMSE score $\pm$ SD	19.6 $\pm$ 10.1	17.7 $\pm$ 6.9	23.3 $\pm$ 7.0
Mean Ham-D score $\pm$ SD ^a	9.2 $\pm$ 7.6	16.2 $\pm$ 9.0	6.9 $\pm$ 4.1
Antidepressant treatment	5 (29.4)	15 (48.4)	8 (57.1)
Hypertension	11 (64.7)	20 (64.5)	9 (64.3)
Stroke	7 (41.2)	9 (29.0)	3 (21.4)
Diabetes	1 (5.9)	5 (16.1)	1 (7.1)
Coronary artery disease	1 (5.9)	5 (16.1)	4 (28.6)
Congestive heart failure	2 (11.8)	7 (22.6)	3 (21.4)
Poor vision	13 (76.5)	21 (67.7)	10 (71.4)
Hearing loss	7 (47.1)	9 (35.5)	7 (50.0)

Values are presented as numbers (%) unless otherwise stated. ^a $F(2, 62) = 6.50$, $p = 0.003$, post hoc details are in the text. All other group effects were nonsignificant (see text).

symptoms including changes in appetite and sleep, fatigue, agitation and trouble concentrating, but did not endorse sadness or anhedonia. Participants were categorized as DD if they presented with emotional symptoms (i.e. sadness, loss of pleasure, or a low sex drive) and other ideational or vegetative symptoms of depression for a total of 5 or more symptoms. The threshold of 5 symptoms was selected so that the DD diagnosis could be comparable to the diagnosis of major depression in the DSM-5 [3]. The ND comparison group included all subjects who did not meet the criteria for NDD or DD.

Descriptive variables included demographics (age, sex, and education), medical conditions (table 1), and the severity of the depressive symptoms (Ham-D) and cognitive impairment (MMSE). Individual depressive symptoms were examined dichotomously. Study hypotheses were examined using SAFE and apathy scores as continuous variables.

Statistical Analysis

Data were analyzed using SAS version 9.2 [39]. Groups were compared using means and standard deviations and one-way ANOVA. Post hoc F tests were used to determine differences between any 2 groups. For nominal variables, groups were compared using Pearson's χ^2 test or Fisher's exact test (if the expected cell size was 5 or less).

Results

Sample Description

The demographic and clinical characteristics of the patients are presented in table 1. The mean age was 87.5 years (SD = 7.7). Thirty-one subjects (50.0%) met the criteria for DD, while 17 subjects (27.4%) met the criteria for NDD. The remainder of the sample ($n = 15$ or 22.6%)

constituted the ND comparison group. There was no significant association between groups and age [$F(2, 62) = 2.16$; $p > 0.05$] or sex ($\chi^2 = 0.87$; $p = 0.65$). In the entire sample, positive correlations between apathy and social functional impairment ($r = 0.54$; $p < 0.01$) and between apathy and cognitive impairment ($r = 0.35$; $p = 0.03$) were found. There was also a positive correlation between apathy and Ham-D scores ($r = 0.57$; $p < 0.0001$). Cognition and social functional adaptation were not significantly correlated.

The group effect for cognitive function did not reach conventional statistical significance [$F(2, 62) = 2.16$; $p = 0.08$]. Post hoc tests (computed for completion based on this nonsignificant trend) showed that DD participants had lower MMSE scores than ND subjects [$F(1, 45) = 6.62$; $p = 0.01$]. The MMSE scores of NDD subjects were not different from those of ND [$F(1, 31) = 1.44$; $p = 0.24$] and DD subjects [$F(1, 45) = 0.58$; $p = 0.45$].

There was a significant group effect for depression severity [$F(2, 62) = 6.50$; $p = 0.003$]. DD subjects had significantly greater Ham-D scores than NDD [$F(1, 48) = 6.06$; $p = 0.02$] and ND participants [$F(1, 45) = 9.09$; $p = 0.005$]. NDD subjects did not differ from ND participants [$F(1, 32) = 0.71$, $p = 0.41$] in terms of Ham-D scores.

The 3 groups did not differ in terms of antidepressant use ($\chi^2 = 1.65$; $p = 0.44$) or the use of other psychotropic medications including lithium ($\chi^2 = 4.96$; $p = 0.09$), sedatives ($\chi^2 = 0.90$; $p = 0.64$), and stimulants ($\chi^2 = 4.17$; $p = 0.12$). There were no statistically significant group effects of stroke ($\chi^2 = 1.73$; $p = 0.42$), hypertension ($\chi^2 = 0.10$; $p =$

Table 2. Emotional, ideational, and vegetative depressive symptoms

Variables	Rate, n (%)			χ^2 value	p
	NDD	DD	ND		
Ideational symptoms					
Guilt	0 (0.0)	3 (9.7)	0 (0)	2.26	0.32
Worthlessness	1 (5.9)	10 (32.33)	0 (0.0)	8.34	<0.05
Hopelessness	13 (76.4)	21 (67.7)	7 (50.0)	5.75	0.05
Suicide thoughts	0 (0.0)	1 (3.2)	0 (0.0)	0.72	0.70
Helplessness ^a	3 (17.6)	30 (96.8)	1 (7.1)	12.99	<0.01
Vegetative symptoms					
Insomnia	5 (31.3)	21 (67.7)	0 (0.0)	0.71	0.69
Fatigue	11 (64.7)	30 (96.8)	6 (42.8)	6.58	0.03
Psychomotor retardation	8 (47.1)	23 (74.2)	2 (14.3)	8.02	0.02
Agitation	2 (11.8)	4 (12.9)	0 (0.0)	1.44	0.49
Poor concentration	4 (23.5)	14 (50.0)	5 (35.8)	1.56	0.12
Loss of appetite	3 (25.5)	9 (32.1)	4 (28.6)	0.21	0.90
Weight loss	1 (5.9)	2 (6.5)	2 (14.3)	2.09	0.35
Other Ham-D symptoms					
Anxiety ^b	2 (11.8)	16 (51.6)	2 (14.3)	6.23	<0.05
Gastrointestinal symptoms	3 (17.6)	9 (29.0)	3 (21.4)	1.30	0.86
General somatic symptoms	0 (0.0)	4 (12.9)	3 (21.4)	5.16	0.08
Diurnal variation of symptoms	3 (17.6)	15 (48.4)	1 (7.1)	5.43	0.07
Depersonalization	1 (5.9)	6 (19.4)	0 (0.0)	3.82	0.25
Paranoid symptoms	13 (76.4)	30 (96.8)	7 (50.0)	5.75	0.05
OCD symptoms	1 (5.9)	3 (9.7)	0 (0.0)	0.94	0.63
Hallucinations	2 (11.8)	6 (19.4)	1 (7.1)	1.45	0.48

OCD = Obsessive-compulsive disorder. ^a Significant difference between NDD and DD, $\chi^2 = 7.38$, $p < 0.01$. ^b Significant difference between NDD and DD, $\chi^2 = 4.97$, $p < 0.05$.

0.95), diabetes ($\chi^2 = 1.56$; $p = 0.46$), coronary artery disease ($\chi^2 = 2.58$; $p = 0.28$), heart failure ($\chi^2 = 0.85$; $p = 0.66$), poor vision ($\chi^2 = 0.49$; $p = 0.78$), or hearing loss ($\chi^2 = 0.84$; $p = 0.65$) (table 1).

Depressive symptoms as a function of depression status are summarized in table 2. There were significant (or near significant; $p = 0.05$) group effects on fatigue, retardation, worthlessness, hopelessness, helplessness, and anxiety. Post hoc analysis showed that between DD and NDD the only DSM-5 symptom that approached statistical significance was worthlessness ($\chi^2 = 2.95$; $p < 0.08$). A near significant effect ($p = 0.05$) was found for paranoid thoughts.

Hypothesis Testing

Apathy had a significant group effect [$F(2, 61) = 24.3$; $p < 0.0001$] (fig. 1). DD subjects showed greater apathy scores relative to NDD [$F(1, 48) = 22.4$; $p < 0.001$] and ND subjects [$F(1, 45) = 71.1$; $p < 0.001$]. NDD subjects did not differ significantly from ND participants [$F(1, 31) = 0.75$; $p > 0.3$] in terms of apathy scores.

SAFE scores also showed a significant effect of group [$F(2, 61) = 7.61$; $p < 0.01$] (fig. 2). Participants with DD showed greater SAFE scores than ND subjects [$F(1, 45) = 12.2$; $p < 0.001$]. Likewise, participants with NDD showed higher SAFE scores relative to ND participants [$F(1, 31) = 3.92$; $p < 0.05$]. There was no significant difference between DD and NDD participants [$F(1, 48) = 1.96$; $p > 0.17$]. The social adaptation domains by group are shown in figure 3.

Discussion

Over one fourth of the oldest old living in nursing home settings reported symptom clusters including ideational and vegetative symptoms of depression (NDD). The most predominant symptoms were hopelessness (>75%), fatigue (>60%), psychomotor retardation (>45%), and paranoia (>75%). Notably, the elevated rate of paranoid symptoms was population specific, as 50% of ND subjects also reported at least one paranoid symptom.

Fig. 1. Apathy score by depression category.

Fig. 2. Functional adjustment score by depression category.

Fig. 3. Functional domain scores by depression category.

The present study did not support the association between NDD and apathy in the nursing home setting. Apathy showed a positive linear association with depression severity. Consistently, group analyses showed greater apathy in DD subjects than in NDD and ND participants.

Whereas by definition NDD can be considered a forme fruste, in terms of associated impairment it behaved more like DD, showing greater social functional impairment relative to ND subjects (and no significant difference in comparison to DD individuals). In addition, al-

though subjects with NDD had generally lower rates of depressive symptoms compared to participants with DD, the two depressive conditions showed no statistically significant difference in DSM-5 depressive symptoms (loss of pleasure and sad mood excluded). These data are consistent with the view that NDD is a phenomenological variant of depression and less so a syndrome related to apathy.

A few caveats must be acknowledged. First, based on the limited sample size, the lack of association between NDD and apathy needs to be considered as preliminary. This sample is largely comprised of the very old; hence, we cannot ascertain if an apathetic NDD may be present among younger individuals (and/or associated with poor longevity) [4]. The cross-sectional design of the present study cannot demonstrate causal associations. Participants with early dementia may have been included but the study population is rather selected, thus limiting generalization to all people living in nursing homes. The symptoms used for subject categorization were assessed using the Hamilton depression scale. Whereas the Hamilton depression scale is most often used to rate the severity of the illness once the diagnosis has already been established, all of the DSM criteria for the diagnosis of depression are present in the scale [35]. In addition, the criteria required to diagnose DD closely resembled major depression criteria. Data on prior depressive episodes were not available. Therefore, whether NDD was a partially treated depression or a depression that never reached the major depression threshold could not be definitely verified. However, the NDD group was the group with the lowest rate (less than 1 in 3) of antidepressant treatment (table 1). This makes it less likely that the participants with NDD had a prior history of depression that was identified and treated. It also reduces the possibility that serotonergic effects (i.e. emotional blunting) of antidepressants determined the nondysphoric presentation of depression [40, 41]. Apathy was assessed using a subscale of the SANS. The SANS was developed and validated for patients with schizophrenia and not for depressed or elderly subjects [37]. More differentiated instruments for the assessment of apathy irrespective of the clinical entity (e.g. Apathy Evaluation Scale) [42, 43] are warranted in future confirmatory research.

The rates of major depression in late life vary depending on the setting. In community-dwelling samples the rate is about 2%, and in primary care the rates fall between 5.0 and 10.0% [44]. In long-term care facilities, the rates range from 15.0 to 40.0% [20, 30, 45]. The rates of DD in the present study were higher than the upper end of the

above spectrum. The rates for NDD were also high (27.4%). Other studies examining younger subjects and community-dwelling samples have reported lower rates (between 5 and 10%) [4, 46–48]. Consistent with the hypothesis suggesting that NDD is frequent among the elderly [12], older age may be a critical factor influencing NDD rates in this study. For some individuals with depression, feelings of sadness (or loss of pleasure) may transitorily enter awareness, be forgotten, and/or not be reported during the clinical exam [4, 12]. Among older adults, age-related changes in brain regions subserving awareness for personal emotions (e.g. the anterior cingulate cortex) may be the neurobiological underpinning of the increased rate of NDD [12, 49].

Consistent with expectations, the ND group was less functionally impaired than both depression groups (NDD and DD) [1, 2, 4, 8, 25]. Similar results have been reported among older nursing home dwellers [27], but no previous study has reported social functional adaptation in older nursing home patients with NDD. In the present study, NDD did not differ from DD in terms of social functional adaptation. Studies on NDD in younger subjects have reported worse functional impairments relative to DD [1, 4]. The reason for this discrepancy [1, 4] may be the greater functional impairment in the present study sample, as poor functioning is often the sole indication for nursing home placement [50, 51].

Other interesting findings in this study were the general associations between apathy and social functional impairment and between apathy and cognitive impairment.

Depressed and ND participants did not vary in terms of the medical burden, thus confirming previous studies [1, 2, 4, 21, 44]. Very old age generally increases the medical burden irrespective of a depression diagnosis, and this may limit depression-based differences in medical status.

Cognitive impairment may be associated with NDD [4, 11, 12, 52–54]. Consistent with earlier research, participants with depression (NDD and DD) showed a non-significant increased likelihood of cognitive impairment compared to ND participants [2, 4, 12, 20, 44, 55] but NDD and DD were not significantly different, a finding that replicates previous research examining older adults in primary care [2]. Further research will need to examine whether cognitive impairment between NDD and DD shows qualitative differences (or differences in distinct cognitive domains).

The rates of paranoid symptoms were high in this sample, consistent with the rates of psychotic symptoms

among nursing home dwellers in other samples [56, 57]. Why paranoid symptoms were elevated in the present study that excluded dementia, bipolar disorder, and schizophrenia may have multifold explanations including hearing deficits and novel environments with rules and regulations that are difficult to adapt to, but also mood disorders.

As expected, subjects with depression (DD and NDD) reported higher rates of anhedonia, anxiety, hopelessness, helplessness, paranoia, fatigue, and worthlessness than ND subjects. Earlier studies have described NDD as subthreshold or subsyndromal depression (by definition not meeting the DSM-5 criteria) [1, 4, 7, 8]. As expected (based on the inclusion criteria), lower Ham-D scores were found among participants with NDD compared to DD [2, 46, 48, 58]. Psychopathological features distinguishing between NDD and DD relative to ND participants included hopelessness, worthlessness, and helplessness. Paradiso et al. [8] reported significant rates of self-depreciation/worthlessness among stroke victims with NDD. The lower likelihood of anxiety in NDD found in the present study is similar to the result of an earlier study by Paradiso et al. [2] and consistent with lower rates of

psychological symptoms including anxiety among elderly with depression [59].

In summary, these findings contribute to the body of literature and further the understanding of late-life depression in nursing homes, giving critical information that is potentially useful for diagnosis and treatment. NDD and DD occurring in late life are more similar than different, with comparable trends in functional impairment. Proper evaluation and treatment of the older old presenting depressive symptoms which do not meet the criteria for a major depressive disorder may potentially reduce functional impairment. As the baby boomers continue to age and the life span further increases, there will be a great need to understand the factors contributing to the development of differing subtypes of depression in late life.

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References

- 1 Lyness JF, Kim J, Tang W, Tu X, Conwell Y, King DA, Caine ED: The clinical significance of subsyndromal depression in older primary care patients. *Am J Geriatr Psychiatry* 2007; 15:214–223.
- 2 Paradiso S, Duff K, Vaidya JG, Hoth A, Mold JW: Cognitive and daily functioning in older adults with vegetative symptoms of depression. *Int J Geriatr Psychiatry* 2010;25:569–577.
- 3 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5). Arlington, APA, 2013, pp 183–184.
- 4 Gallo JJ, Rabins PV, Lyketsos CG, Tien AY, Anthony JC: Depression without sadness: functional outcomes of nondysphoric depression in later life. *J Am Geriatr Soc* 1997;45: 570–578.
- 5 Gotfries C: Late life depression. *Eur Arch Psychiatry Clin Neurosci* 2001;251(suppl 2):II57–II61.
- 6 Meller I, Fichter M, Schroppel H: Incidence of depression octogenarians and nonagenarians: result of an epidemiological follow-up-community study. *Euro Arch Psychiatr Neurol* 1996;246:93–99.
- 7 Paradiso S, Caspers K, Tranel D, Coryell W: Cognitive and nondysphoric depression among adoptees at high risk for psychopathology. *Compr Psychiatry* 2011;52:498–506.
- 8 Paradiso S, Vaidya J, Tranel D, Kosier T, Robinson R: Nondysphoric depression following stroke. *J Neuropsychiatry Clin Neurosci* 2008;20:52–61.
- 9 Canto J, Shilpak M, Rogers W, Malmgren J, Frederick P, Lambrew C, Ornato J, Barron H, Kiefe C: Prevalence, clinical characteristics, and mortality among patients with myocardial infarction presenting without chest pain. *JAMA* 2000;283:3223–3229.
- 10 Ahkee S, Srinath L, Ramirez J: Community-acquired pneumonia in the elderly: association of mortality with lack of fever and leukocytosis. *South Med J* 1997;90:296–298.
- 11 Chuan SK, Kumar R, Matthew N, Hoek KE, Pin NT: Subsyndromal depression in old age: clinical significance and impact in a multi-ethnic community sample of elderly Singaporeans. *Int Psychogeriatr* 2008;20: 188–200.
- 12 Paradiso S, Vaidya JG, McCormick LM, Jones A, Robinson RG: Aging and alexithymia: association with reduced right rostral cingulate volume. *Am J Geriatr Psychiatry* 2008;16: 760–769.
- 13 Beekman A, Copeland J, Prince M: Review of community prevalence of depression in late life. *B J Psychiatry* 1999;174:307–311.
- 14 Blazer D: Depression in late life: a review and commentary. *J Gerontol A Biol Sci Med Sci* 2003;58:249–265.
- 15 Mulsant BH, Ganguli M: Epidemiology and diagnosis of depression in late life. *J Clin Psychiatry* 1999;60:9–15.
- 16 Ishii S, Weintraub N, Mervis J: Apathy a common psychiatric syndrome in the elderly. *J Am Med Dir Assoc* 2009;10:381–393.
- 17 Kales H, Chen P, Blow F, Welsh D, Mellow A: Rates of clinical depression diagnosis, functional impairment and nursing home placement in coexisting depression and dementia. *Am J Geriatr Psychiatry* 2005;13: 441–449.
- 18 Mehta M, Whyte E, Lenze E, Hardy S, Roumani Y, Subashan P, Huang W, Studenski S: Depressive symptoms in late life: associations with apathy, resilience and disability vary between young-old and old-old. *Int J Geriatr Psychiatry* 2004;23:238–243.
- 19 Onyike C, Sheppard J, Tschanz J, Norton M, Green R, Steinberg M, Welsh-Bohmer K, Breitner J, Lyketsos C: Epidemiology of apathy in older adults: the Cache County Study. *Am J Geriatr Psychiatry* 2007;15:365–375.
- 20 Payne J, Sheppard J, Steinberg M: Incidence, prevalence and outcomes of depression in residents of long-term care facility with dementia. *Intl J Geriatr Psychiatry* 2002;17:247–253.
- 21 Starkstein SE, Fedoroff JP, Price TR, Leiguarda R, Robinson RG: Apathy following cerebrovascular lesions. *Stroke* 1993;24:1625–1630.

- 22 Yamagata S, Yamaguchi S, Kobayashi S: Impaired novelty processing in apathy after subcortical stroke. *Stroke* 2004;35:1935–1940.
- 23 Wells K, Stewart A, Hays R, Burnam M, Rogers W, Daniels M, Berry S, Greenfield S, Ware J: The functioning and well-being of depressed patients: results from the medical outcome study. *JAMA* 1989;262:914–919.
- 24 Hirschfeld R, Montgomery S, Keller M, Kasper S, Schatzberg A, Möller H, Healy D, Baldwin D, Humble M, Versiani M, Montenegro R, Bourgeois M: Social functioning in depression: a review. *J Clin Psychiatry* 2000; 61:268–275.
- 25 Glass T, Mendes de Leon C, Bassuk S, Berkman L: Social engagement and depressive symptoms in late life. *J Aging Health* 2006;18: 604–628.
- 26 Weissman M, Bothwell S: Assessment of social judgment by patient self-report. *Arch Gen Psychiatry* 1976;33:1111–1115.
- 27 Achterberg W, Pot A, Kerkstra A, Ooms M, Muller M, Ribbe M: The effect of depression on social engagement in newly admitted Dutch nursing home residents. *Gerontologist* 2003;43:213–218.
- 28 Brodaty H, Draper B, Saab D, Low LF, Richards V, Paton H, Lie D: Psychosis, depression and behavioural disturbances in Sydney nursing home residents: prevalence and predictors. *Int J Geriatr Psychiatry* 2001;16:504–512.
- 29 Byrne GJ, Pachana NA: Anxiety and depression in the elderly: do we know any more? *Curr Opin Psychiatry* 2010;23:504–509.
- 30 Thakur M, Blazer G: Depression in long-term care. *J Am Med Dir Assoc* 2008;9:82–87.
- 31 Penninx BW, Guralnik JM, Ferrucci L, et al: Depressive symptoms and physical decline in community-dwelling older persons. *JAMA* 1998;279:1720–1726.
- 32 Onwuameze O, Schultz S, Paradiso S: An initial study of modifiable and non-modifiable factors for late life psychosis. *Int J Psychiatry Med* 2011;42:437–451.
- 33 Schultz SK, Ellingrod VL, Moser DJ, Kutschner E, Turvey C, Arndt S: The influence of cognitive impairment and psychiatric symptoms on daily functioning in nursing facilities: a longitudinal study. *Ann Clin Psychiatry* 2002;14:209–213.
- 34 Schultz SK, Ellingrod VL, Turvey C, Moser DJ, Arndt S: The influence of cognitive impairment and behavioral dysregulation on daily functioning in the nursing home setting. *Am J Psychiatry* 2003;160:583–584.
- 35 Hamilton M: Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol* 1967;6:278–296.
- 36 Folstein MF, Folstein SE, McHugh PR: 'Minimal mental state': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;23:189–198.
- 37 Andreasen NC: Negative symptoms in schizophrenia: definition and validation. *Arch Gen Psychiatry* 1982;39:784–788.
- 38 Harvey PD, Davidson M, Mueser KT, Parella M, White L, Powchik P: Social-Adaptive Functioning Evaluation (SAFE): a rating scale for geriatric psychiatric patients. *Schizophr Bull* 1997;23:131–145.
- 39 SAS Institute: SAS Version 9.2 Cary, SAS Institute, 2008.
- 40 McCabe C, Mishor Z, Cowen P, Harmer C: Diminished neural processing of aversive and rewarding stimuli during selective serotonin reuptake inhibitor treatment. *Biol Psychiatry* 2010;67:439–445.
- 41 Sansone R, Sansone L: SSRI-induced indifference. *Psychiatry* 2010;7:14–18.
- 42 Marin R, Biedrzycki R, Firinciogullari S: Reliability and validity of the apathy evaluation scale. *Psychiatry Res* 1991;38:143–146.
- 43 Starkstein S, Petracca G, Chemerinski E, Janus K: Syndromic validity of apathy in Alzheimer's disease. *Am J Psychiatry* 2001;158: 872–877.
- 44 Lyness J, Caine E, King D, Conwell Y, Cox C, Yoediono Z: Psychiatric disorders in older primary care patients. *J Gen Intern Med* 1999; 14:249–254.
- 45 Boswell E, Stoudemire A: Major depression in the primary care setting. *Am J Med* 1996;101: 3S–9S.
- 46 Backenstrass M, et al: Preferences for treatment in primary care: a comparison of non-depressive, subsyndromal and major depressive patients. *Gen Hosp Psychiatry* 2006;28: 178–180.
- 47 Judd LL, Akiskal HS, Paulus MP: The role and clinical significance of subsyndromal depressive symptoms (SSD) in unipolar major depressive disorder. *J Affect Disord* 1997;45:5–18.
- 48 Judd LL, et al: Subsyndromal symptomatic depression: a new mood disorder? *J Clin Psychiatry* 1994;55:18–28.
- 49 Koenigs M, Huey ED, Calamia M, Raymond V, Tranel D, Grafman J: Distinct regions of prefrontal cortex mediate resistance and vulnerability to depression. *J Neurosci* 2008;28: 12341–12348.
- 50 Smith GE, Kokmen E, O'Brien PC: Risk factors for nursing home placement in a nursing home dementia cohort. *J Am Geriatr Soc* 2000;48:519–525.
- 51 Yaffe K, Fox P, Newcomer R, Sands L, Lindquist K, Dane K, Covinsky KE: Patient and caregiver characteristics and nursing placement in patients with dementia. *JAMA* 2002;287:2090–2097.
- 52 Brown MN, Lapane KL, Luisi AF: The management of depression in older nursing home residents. *J Am Geriatr Soc* 2002;50:69–76.
- 53 Kohler S, van Bortel MP, van Os J, Thomas AJ, O'Brien JT, Jolles J, Verhey FRJ, Allardyce J: Depressive symptoms and cognitive decline in community-dwelling older adults. *J Am Geriatr Soc* 2010;58:873–879.
- 54 Kohler S, Thomas AJ, Lloyd A, Barber R, Almeida OP, O'Brien JT: White matter hyperintensities, cortisol levels, brain atrophy and continuing cognitive deficits in late-life depression. *Br J Psychiatry* 2010;196:143–149.
- 55 Taresi J, Abrams R, Holmes D, Ramirez M, Eimicke J: Prevalence of depression and depression recognition in nursing homes. *Soc Psychiatry Psychiatr Epidemiol* 2001;36:613–620.
- 56 Ropacki SA, Jeste DV: Epidemiology and risk factors for psychosis of Alzheimer's disease: a review of 55 studies published from 1990–2003. *Am J Psychiatry* 2005;162:2022–2030.
- 57 Zuidema SU, Derksen E, Verhey FRJ, Koopmans RTC: Prevalence of neuropsychiatric symptoms in a large sample of Dutch nursing home patients with dementia. *Int J Geriatr Psychiatry* 2007;22:632–638.
- 58 Lyness JM, Heo M, Datto CJ, Ten Have TR, Katz IR, Drayer R, Reynolds CF, Alexopoulos GS, Bruce ML: Outcomes of minor and subsyndromal depression among elderly patients in a primary care setting. *Ann Intern Med* 2006;144:496–504.
- 59 Simon G, Vonkorff M, Piccinelli M, Fullerton C, Ormel J: An international study of the relationship between somatic symptoms depression. *N Engl J Med* 1999;341:1329–1335.